Remarks

Upon entry of the amendments, claims 1, 15-20, 26-27, 31-50, 53-56, 63 and 68-83 will be pending. Claims 10-13 were previously canceled without prejudice or disclaimer. Claims 1 and 81 have been amended for clarification. No new matter has been added.

Elections/Restrictions

In addition to withdrawing claims 19-20, 39-50, 54-56, 76, and 79-80 as directed to non-elected subject matter, the Examiner has now withdrawn claims 63 and 82-83. *See* Office Action at pages 2-3. Applicants contend that claim 63 is directed to the invention elected in the Response filed November 18, 2005, in which SEQ ID NO:24 (a peptide derived from a human neurokinin receptor) was provisionally elected. Accordingly, Applicants request that the Examiner consider this claim pending and under examination.

Applicants further request that claims 82 and 83 (drawn to non-elected species) be examined upon allowance of a generic claim. Applicants maintain their previous request that the withdrawn process claims, which depend (directly or indirectly) from and necessarily include all the limitations of elected product claim 1, be rejoined in accordance with the provisions of MPEP § 821.04.

Indefiniteness

Applicants acknowledge with appreciation the Examiner's withdrawal of the rejection of claim 34 for indefiniteness.

Novelty

Claims 1, 15-18, 26, 31-32, 53, and 81 are rejected under 35 U.S.C. § 102(b) as anticipated by Schilfgaarde. According to the Examiner, Schilfgaarde discloses a penetrating peptide sequence (SEQ ID NO:4) that comprises SEQ ID NO:1 of the instant application. The

Examiner posits that amino acid residues 1-2 or 26-205 of Schilfgaarde's SEQ ID NO:4 could serve as an effector molecule that is fused to the penetrating peptide sequence of SEQ ID NO:1 (denoted by amino acids 3-25 of Schilfgaarde's SEQ ID NO:4) and that such a structure would encompass, and thus anticipate, a penetrating module as recited by claim 1. *See* Office Action at pages 3-4. Applicants traverse.

Independent claims 1 and 81 (from which all other claims subject to the rejection directly or indirectly depend) recite, in relevant part, a penetrating module comprising an effector that is coupled or fused to a penetrating peptide consisting of at least one amino acid sequence selected from the group consisting of SEQ ID NOS: 1-15 and 24-29. As detailed by the instant specification the terms "fusion," "fused," "coupled" or "attached" refers to specific interactions that result in two or more separate molecules showing a preference for one another relative to some third molecule. *See* specification at page 8, lines 1-5; *see also* specification page 18, lines 19-21. Thus, Applicants submit that the specification makes clear that the penetrating module is a conjugate between at least two compounds - *e.g.*, the effector and the penetrating peptide - from different origin, which are then paired together. In one embodiment, the effector can be paired with the penetrating peptide via a peptide linker. *See* specification at page 16, lines 5-10; and page 17, lines 12-15. Accordingly, the penetrating module is chimeric in nature, as demonstrated by Examples 1-10 on pages 33-44 of the instant specification.

In contrast, amino acid residues 1-25 or 3-205 of Schilfgaarde's SEQ ID NO:4 (a portion of which forms the penetrating peptide sequence SEQ ID NO: 1 recited by the claimed invention) cannot be interpreted as a penetrating module comprising a conjugate between an effector and a penetrating peptide, which show a preference for one another relative to some other molecule in accordance with the claimed invention. Rather, amino acid residues 1-25 or 3-205 of Schilfgaarde's SEQ ID NO:4 are simply contiguous amino acid residues from the same origin. While the effector portion of the penetrating module of the claimed invention can include, *inter alia*, DNA, RNA, or proteins (*see* specification at page 18, lines 1-9), Applicants contend that the specification makes clear that such DNA, RNA, or proteins are not derived from the same origin as is the penetrating peptide.

Accordingly, because Schilfgaarde does not teach or suggest all the limitations of independent claims 1 and 81, Applicants contend that Schilfgaarde cannot anticipate these claims. Similarly, because claims 15-18, 26, 31-32, and 53 depend directly or indirectly from

claim 1 and necessarily incorporate all the limitations thereof, Schilfgaarde cannot anticipate these claims either. Thus, this rejection should be withdrawn.

Obviousness

The Examiner rejects claims 1, 15-18, 26-27, 31-38, 53, 68-75, 77-78, and 81 under 35 U.S.C. § 103(a) as obvious in view of Schilfgaarde in view of Juliano in view of Lindgren, and further in view of Veronese for the reasons previously made of record in the Office Action mailed 2/7/06. According to the Examiner, it would have been obvious to one of ordinary skill in the art to combine the teachings of Schilfgaarde, Lindgren, Juliano, and Veronese to design a penetrating module comprising a penetrating peptide conjugated to an effector molecule for transporting biologically active molecules across membranes. *See* Office Action of 2/7/06 at pages 4-6. Applicants reiterate their earlier arguments, which addressed the combination of references.

As discussed above, independent claims 1 and 81 (from which all other claims subject to the rejection directly or indirectly depend) recite, in relevant part, a penetrating module comprising an effector that is coupled or fused to a penetrating peptide consisting of at least one amino acid sequence selected from the group consisting of SEQ ID NOS: 1-15 and 24-29.

A rejection under 35 U.S.C. § 103 cannot be predicated on the mere identification of individual components of the claimed invention in the prior art. Rather, in order for an obviousness rejection to be proper, there must be a teaching or suggestion within the prior art that motivates the ordinarily skilled artisan at the time of invention to modify or combine the references to achieve the claimed invention with a reasonable expectation of success. These requirements are lacking here.

While Schilfgaarde teaches an amino acid sequence (SEQ ID NO:4) comprising SEQ ID NO: 1 of the claimed invention, Schilfgaarde does not teach or suggest that a peptide consisting of amino acid residues 3-25 of its SEQ ID NO:4 (corresponding to SEQ ID NO: 1 of the claimed invention) is useful for translocating a biologically active effector molecule coupled thereto across a biological barrier. Nor does Schilfgaarde suggest that its full-length amino acid sequence of SEQ ID NO:4 be modified in a manner required to meet the invention

as recited by independent claims 1 and 81. To the contrary, Applicants assert that one of skill in the art reading Schilfgaarde at the time of invention would be led to understand that the full-length sequence of Schilfgaarde's SEQ ID NO:4 is required for penetration through epithelial cell layers. Accordingly, Schilfgaarde actually teaches away from the claimed invention, which recites, in relevant part, a penetrating peptide consisting of SEQ ID NO:1 (corresponding to the amino acid residues 3-25 of Schilfgaarde's SEQ ID NO:4). Furthermore, Schilfgaarde does not teach or suggest any of the other penetrating peptides of SEQ ID NOS: 2-15 and 24-29.

Moreover, with regard to the combination of Schilfgaarde with Lindgren, Juliano, and Veronese, Applicants assert that the Examiner improperly relies on hindsight reconstruction. The mere fact that references can be combined or modified to fit the claimed invention does not render the resultant combination obvious unless the prior art references themselves suggest the desirability of the combination. *See In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Here, there is no suggestion or motivation in Lindgren, Juliano, and Veronese to combine their collective teachings with Schilfgaarde to achieve the claimed invention. Applicants contend that the one paragraph reasoning relied on by the Examiner in order to establish the motivation to modify the references (*see* Office Action of 2/7/06 at page 6) is too conclusory and does not point to an explicit or implicit suggestion or motivation within the cited references. *See* MPEP § 2143.01.

Arguendo, even if there was a suggestion or motivation to combine Juliano, Lindgren, and/or Veronese with Schilfgaarde (and there is not), the combination does not cure the deficiencies in the teachings of Schilfgaarde. Although Juliano and Lindgren teach or suggest the use of cell penetrating peptides conjugated to biologically active peptides or proteins, and Veronese teaches pegylation of biologically active peptides or proteins for advantageous pharmacokinetics, none of these references specifically identify amino acid sequences consisting of SEQ ID NOS: 1-15 and 24-29 for use as the penetrating peptide that is conjugated to the biologically active effector molecule. Accordingly, even if these references were properly combined by one of ordinary skill in the art at the time of invention, their combined teachings still do not teach or suggest all of the limitations of the claims as amended herein.

Furthermore, it is not apparent from the Examiner's rejection why one of ordinary skill in the art at the time of invention relying on any of the cited references, alone or in

combination, would have a reasonable expectation of success in achieving the claimed invention since none of the references teach or suggest using a sequence consisting of amino acid residues 3-25 of Schilfgaarde's SEQ ID NO:4 to enhance penetration of a conjugated effector molecule across a biological barrier .

For the foregoing reasons, Applicants contend that independent claims 1 and 81 are non-obvious in view of the combination of cited references. Similarly, because the remaining claims subject to the rejection each depend directly or indirectly from claim 1, these claims are also non-obvious in view of the combination of cited references. Reconsideration and withdrawal of the rejection are requested.

Double Patenting

Claims 1, 31, 33, 34, and 53 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1, 2, 90, 97, 101 and 102 of co-pending U.S. Application No. 10/665,184 (Attorney Docket No. 24348-501 CIP). Additionally, claims 1, 32, 35, 77, and 78 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1, 44, 64-68, 72, and 73 of co-pending U.S. Application No. 10/942,300 (Attorney Docket No. 24348-503). According to the Examiner, the claims of the instant application are claiming common subject matter to those claims referenced in the co-pending applications.

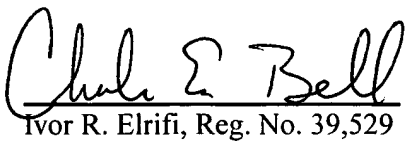
Applicants will file a terminal disclaimer in compliance with 37 C.F.R. 1.321 (c) upon notification of allowable subject matter.

Conclusion

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

With no extension of time this response is due on or before August 28, 2006 (the nominal due date of August 26, 2006 occurring on a Saturday). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 24348-501 NATL.

Respectfully submitted,



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